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TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT REPELLENT--ETC(U)
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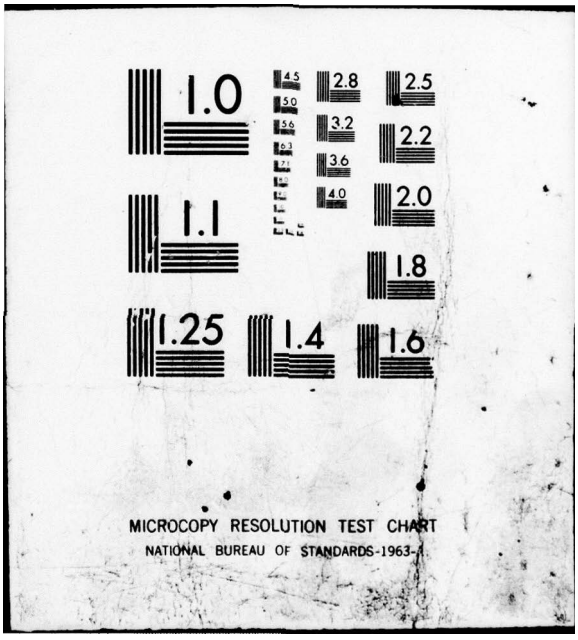
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UNITED STATES ARMY ENVIRONMENTAL HYGIENE AGENCY

ABERDEEN PROVING GROUND, MD 21010

AEHA

TOPICAL HAZARD EVALUATION PROGRAM
OF CANDIDATE INSECT REPELLENT AI3-36317
US DEPARTMENT OF AGRICULTURE PROPRIETARY COMPOUND
~~STUDY NO. 75-51-0872-79~~
MAY 1976 - JUNE 1979.

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20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

A hazard evaluation of candidate insect repellent AI3-36317 was performed by means of laboratory studies using rats, rabbits, and guinea pigs. The technical grade compound caused mild corneal and conjunctival irritation and stained the skin of rabbits. It did not produce photo irritation, did not sensitize guinea pigs, and did not prove to be an acute ingestion hazard.

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U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010

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SUBJECT: Topical Hazard Evaluation Program of Candidate Insect Repellent AI3-36317, US Department of Agriculture Proprietary Compound, Study No. 75-51-0872-79, May 1976 - June 1979

Executive Secretary
Armed Forces Pest Control Board
Forest Glen Section, WRAMC
Washington, DC 20012

A summary of the pertinent findings and recommendations of the inclosed report follows:

A hazard evaluation of candidate insect repellent AI3-36317 was performed by means of laboratory studies using rats, rabbits, and guinea pigs. The technical grade compound caused mild corneal and conjunctival irritation and stained the skin of rabbits. It did not produce photo irritation, did not sensitize guinea pigs, and did not prove to be an acute ingestion hazard. Based on the skin staining properties, it was recommended that AI3-36317 not be approved for further testing as a candidate insect repellent. If the staining properties would pose no problem at proposed use formulations (as a cloth impregnant, for example), it is recommended that AI3-36317 be resubmitted in this form for further testing.

FOR THE COMMANDER:

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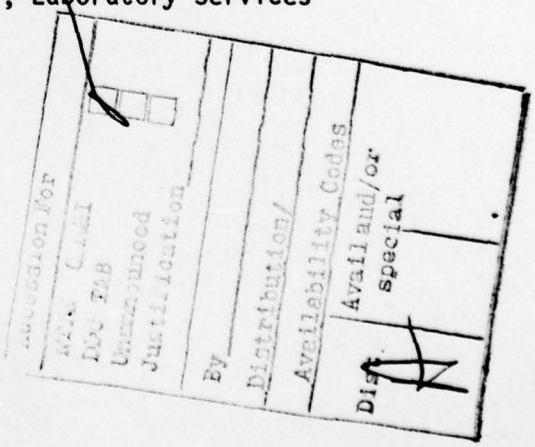

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TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT REPELLENT AI3-36317 US DEPARTMENT OF AGRICULTURE PROPRIETARY COMPOUND STUDY NO. 75-51-0872-79 MAY 1976 - JUNE 1979

1. AUTHORITY.

a. Memorandum of Understanding between the Department of the Army Office of The Surgeon General; the US Army Health Services Command; the US Army Environmental Hygiene Agency; the Armed Forces Pest Control Board; and the US Department of Agriculture, Agriculture Research Service; effective 1970 with Amendment No. 1, effective August 1974.

b. Letter, US Department of Agriculture - Agriculture Research Service, Southern Region, Insects Affecting Man - Research Laboratory, Gainesville, Florida, 5 May 1976.

2. REFERENCE. Toxicology Division Procedural Guide, US Army Environmental Hygiene Agency (USAEHA), 1972, revised 1976.

3. PURPOSE. The purpose of this program is to provide guidance for further entomological testing of the candidate insect repellent AI3-36317.

4. SUMMARY OF FINDINGS. A hazard evaluation of the candidate insect repellent AI3-36317, USDA Proprietary Compound, was conducted by this Agency using New Zealand White rabbits for skin and eye studies, Hartley guinea pigs for a skin sensitization study and Sprague-Dawley rats for determination of oral toxicity. A tabular presentation of animal toxicity data developed in this Agency follows.*†

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* In conducting the studies described in this report, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals," US Department of Health, Education and Welfare Publication No. (NIH) 74-23, revised 1972 - second printing 1974.
† The experiments reported herein were performed in animal facilities fully accredited by the American Association for Accreditation of Laboratory Animal Care.

Study No. 75-51-0872-79, May 76 - Jun 79

Test	Results	Interpretation
SKIN IRRITATION STUDIES		
Rabbits		
Single 24-hour application to intact and abraded skin of New Zealand White Rabbits.		
0.5 g technical grade compound applied to each of six rabbits as a solid	Applied as a brown crystalline solid., AI3-36317 did not produce any primary irritation of intact or abraded skin.	USAEHA Category I (ref Appendix)
0.5 ml of a mixture containing 3 g compound and 1 ml acetone applied to each of six rabbits.	Applied dissolved in 1 ml of acetone, AI3-36317 produced a brown stain which persisted at 72 hours.	USAEHA Category V (ref Appendix)
EYE IRRITATION STUDIES		
Rabbits		
Single 24-hour application of 0.1 g technical grade compound to one eye of each of six New Zealand White Rabbits.	Compound AI3-36317 produced mild injury to the cornea and conjunctiva in one of six rabbits.	USAEHA Category C (ref Appendix)
APPROXIMATE LETHAL DOSE (ALD)		
Oral		
Rats (male) corn oil diluent	ALD >2200 mg/kg	Presents little lethal hazard from acute accidental ingestion.

Study No. 75-51-0872-79, May 76 - Jun 79

Test	Results	Interpretation
PHOTOCHEMICAL SKIN IRRITATION STUDIES		
Rabbits		
A 0.05 ml application of a 25 percent (w/v) solution of the compound and of a 10 percent (w/v) oil of Bergamot solution* in 95 percent ethyl alcohol, was applied to the intact skin of six rabbits. Five minutes after application, the rabbits were exposed to UV light (365 nm) for 30 minutes at a distance of 10-15 cm.	A 25 percent solution of AI3-36317 in ethanol did not cause a photochemical skin irritation reaction under test conditions.	Compound AI3-36317 did not cause a photochemical irritation reaction under test conditions and is not expected to cause a photochemical irritation in humans.
	Positive control application and irradiation caused greater irritant effects than in unirradiated skin area.	
Control		
Following UV exposures of the rabbits, 0.05 ml of test compound, positive control, and diluent were applied to additional skin areas to serve as unirradiated control sites. Application areas were checked for skin irritation reactions at 24, 48 and 72 hours.		

* positive control

Study No. 75-51-0872-79, May 76 - Jun 79

Test	Results	Interpretation
SENSITIZATION STUDIES		
Guinea Pigs		
Intradermal injections of 0.1 ml of a 0.1 percent suspension (w/v) of AI3-36317 or of dinitrochlorobenzene (DNCB)* in a mixture containing 1 volume of propylene glycol and 29 volumes of saline.		
Ten test guinea pigs were given 10 sensitizing doses over a 3-week period. After 2 weeks' rest, they were challenged with a 0.1 percent solution of AI3-36317.	Challenge dose of test compound (last intradermal injection) did not produce a sensitization reaction.	Compound AI3-36317 did not produce a sensitization reaction under these test conditions and is not expected to produced a sensitization reaction in man.
Ten positive control guinea pigs were given 10 sensitizing doses of DNCB over a 3-week period. After 2 weeks' rest, they were challenged with a 0.1 percent suspension of DNCB.	Positive control (DNCB) produced a marked sensitization reaction in 9 of 10 guinea pigs.	

* A known skin sensitizer.

5. CONCLUSION. The candidate insect repellent AI3-36317 has a potential for causing mild corneal and conjuctival irritation and staining the skin. It presents no hazard to the skin when applied as a solid, and did not cause photo irritation. It did not sensitize guinea pigs or prove to be an acute ingestion hazard.

6. RECOMMENDATION. Under the provisions of the Memorandum of Understanding (paragraph 1a), it is recommended that AI3-36317, USDA Proprietary Compound, not be approved for further testing as a candidate insect repellent, since it is unsuitable for application to human skin. If, however, it can be formulated as an impregnant, so that staining would not be a problem, it is suggested this formulation be resubmitted for further evaluation.

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APPENDIX

TOPICAL HAZARD EVALUATION PROGRAM
DEFINITIONS OF CATEGORIES OF COMPOUNDS BEING CONSIDERED FOR ACUTE SKIN APPLICATION

CATEGORY I - Compounds producing no primary irritation of the intact skin or no greater than mild primary irritation of the skin surrounding an abrasion. (INTERPRETATION: No restriction for acute application to the human skin.)

CATEGORY II - Compounds producing mild primary irritation of the intact skin and the skin surrounding an abrasion. (INTERPRETATION: Should be used only on human skin found by examination to have no abrasions or may be used as a clothing impregnant.)

CATEGORY III - Compounds producing moderate primary irritation of the intact skin and the skin surrounding an abrasion. (INTERPRETATION: Should not be used directly on the skin without a prophetic patch test having been conducted on humans to determine irritation potential to human skin. May be used without patch testing, with extreme caution, as clothing impregnants. Compound should be resubmitted in the form and at the intended use concentration so that its irritation potential can be reexamined using other test techniques on animals.)

CATEGORY IV - Compounds producing moderate to severe primary irritation of the intact skin and of the skin surrounding an abrasion and, in addition, producing necrosis, vesiculation, and/or eschars. (INTERPRETATION: Should be resubmitted for testing in the form and at the intended use concentration. Upon resubmittion, its irritation potential will be reexamined using other test techniques on animals, prior to possible prophetic patch testing in humans, at concentrations which have been shown not to produce primary irritation in animals.)

CATEGORY V - Compounds impossible to classify because of staining of the skin or other masking effects owing to physical properties of the compound. (INTERPRETATION: Not suitable for use on humans.)

EYE CATEGORIES:

A. Compounds noninjurious to the eye. INTERPRETATION: Irritation of human eyes is not expected if the compound should accidentally get into the eyes, provided it is washed out as soon as possible.

B. Compounds producing mild injury to the cornea. INTERPRETATION: Should be used with caution around the eyes.

C. Compounds producing mild injury to the cornea, and in addition some injury to the conjunctiva. INTERPRETATION: Should be used with caution around the eyes and mucosa.

D. Compounds producing moderate injury to the cornea. INTERPRETATION: Should be used with extreme caution around the eyes.

E. Compounds producing moderate injury to the cornea, and in addition producing some injury to the conjunctiva. INTERPRETATION: Should be used with extreme caution around the eyes and mucosa.

F. Compounds producing severe injury to the cornea and to the conjunctiva. INTERPRETATION: Should be used with extreme caution. It is recommended that use be restricted to areas other than the face.